DETAILED ACTION

Claims 1-46 are pending. Claims 1-7 are considered on the merits. Species election of lipase is acknowledged. Claims 8-46 are withdrawn from consideration as being drawn to a non-elected invention.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

INDEFINITE

Claim 5 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 states that the enzyme is part of a whole cell culture. This claim is not clear because it cannot be understood if applicants are attempting to claim that the enzyme is from a microbe or animal. Also unclear is if the intact cell is meant to be a part of the reaction or if just the enzyme which is obtained from a microbial or animal culture is in the reaction mixture. It is noted that upon clarification of this claim, if it reads on the incorporation of an intact mammalian or other higher animal cell, a scope of enablement rejection may be instituted as there do not appear to be any examples in the literature which use intact higher animal cells to catalyze these types of reactions. What is unknown is unpredictable by definition. Please be careful not to add new matter. Please point to the place in the as-filed specification where support for any amendment exists.

Response to Arguments

Applicants argue that the enzymes may be part of a whole cell culture such as a live cell culture.... however, it is uncertain if the recitation includes the use of mammalian, insect, plant cell cultures or is limited to microbial cultures.

Claim Rejections - 35 USC § 103

Claims 1-4, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/42687 [2] in light of Beier *et al.* [U].

The claims are directed to an enzymatic catalytic process comprising reacting a substrate with a biological catalyst (lipase has been elected) in a solvent comprising at least one hydrofluorocarbon and water in a concentration less than saturation of the hydrofluorocarbon (one phase) to stereoselectively form a product.

The references are relied upon as explained below.

WO 98/42687 discloses the use of trifluoromethane (page 24, l.5) as a solvent in lipase catalyzed stereochemical reactions (abstract).
While there is no mention of the water content of the reaction, lipase preparations always contain some water as explained by Beier *et al.*, page 1680, first column, second paragraph.

Claim 6 remains rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/42687 [2], Bier *et al.* [U] as applied to claims 1-4, 7 above, and further in view of Janda *et al.* [V].

The claims are further directed to the use of an abzyme as the biological catalyst.

Janda *et al.* disclose that abzymes (catalytic antibodies) are known having acyl transfer and peptide cleavage activities among others.

It would have been obvious to substitute an abzyme for the enzyme disclosed in the process of WO 98/42687 because Janda *et al.* teach that such catalytic antibodies can be engineered to have lipase, protease, oxidoreductase and other activities. Thus, one of skill in the art may create an abzyme with the desired characteristics in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed 1/26/10 have been fully considered but they are not persuasive.

Applicant argues that WO 98/42687 does not teach the use of hydrofluorocarbon solvent in preference to any of the numerous other solvents said to be suitable and that biphasic solvent systems are also contemplated. Water and mixture of water and organic solvents are preferred and when a water/organic mixture is used, the organic solvent is within the range of 0-95%.

While the reference teaches the preference of water/organic solvent mixtures, it also teaches the use of organic solvents alone, "A given reaction **may also** be carried out in a biphasic system…" (page 23, l. 29), thus the reference teaches the use of both biphasic systems and monophasic organic solvents which includes halogenated solvents such as trifluoromethane. What is most likely is not the same as a teaching away from the claimed invention.

It is acknowledged that the prior art as a whole must suggest the desirability of the invention, but a finding that the prior art as a whole suggests the desirability of a particular combination need not be supported by a finding that the prior art suggests that the combination claimed is the preferred, or most desirable combination. The prior art's mere disclosure of more than one alternative does not constitute a teaching away from the claimed invention because such disclosure does not criticize, discredit, or other wise discourage the solution claimed in the patent application. See *In re* Fulton, 391 F.3d 1195, 73 USPQ2d 1411 (2004).

Applicants argue that Beier *et al.* would provide the skilled person with no motivation to use hydrofluorocarbons in an enzymatic reaction. Please see how the reference of Beier *et al.* was relied upon, "lipase preparations always contain some water as explained by Beier *et al.*, page 1680, first column, second paragraph.". Also, please observe the construction of the rejection where the

primary reference of WO 98/42687 is taken IN LIGHT OF Beier *et al.*, not in combination with. Thus, the combination of a hydrofluorocarbon solvent and an enzyme always contains some water. This is inherent in the combination. Since the claims only contain an upper concentration limit to the water, the combination of an enzyme and a hydrofluorocarbon as disclosed in WO 98/42687 fulfills the claimed limitation.

Applicant argues that Janda *et al.* provide no teaching of the use of an abzyme in a hydrofluorocarbon solvent. While this is true, please look above at the reason that was relied upon for the citation of Janda *et al.* The reference teaches that catalytic antibodies can have lipase activity and enantioselectivity. Therefore, it would be obvious to substitute such a catalytic antibody for a lipase enzyme since the catalytic activity is the same.

Claims 1-5, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,925,790 [A] and Ferraboschi *et al.* [X].

The claims have been discussed above.

The references are relied upon as explained below.

US 4,924,790 disclose the use of trifluoromethane (col. 2 l. 61) as a reaction solvent for enzymatic reactions. Water will be present in the reaction mixture (col. 2, l. 49). Any enzyme may be used which include those useful in the production of pharmaceuticals (col. 3, l. 20) particularly with steroids (col. 3, l. 27). Thus, since reactions with enzymes commonly include stereospecific reactions, this generic disclosure inherently invites stereospecific enzymatic reactions.

Ferraboschi *et al.* disclose the use of a lipase in a stereospecific resolution of a steroid, 26-hydroxycholesterol, which has both R and S epimers.

The substitution of the hydrofluorocarbon solvent, trifluoromethane as disclosed in US 4,925,790 for the solvent in the lipase catalyzed reaction of Ferraboschi *et al.* would have been obvious because US 4,925,790 specifically invites the use of the hydrofluorocarbon solvent.

With regard to the limitation "enantiomeric success greater than 50%", in the absence of specifics of the reaction is merely a desired result and thus has little patentable weight in the instant recitations.

Claim 6 remains rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,924,790 [A] and Ferraboschi *et al.* [X] as applied to claims 1-5, 7 above, and further in view of Janda *et al.* [V].

Janda *et al.* has been discussed above.

It would have been obvious to substitute an abzyme for the enzyme disclosed in the process of US 4,924,790 [A] because Janda *et al.* teach that such catalytic antibodies can be engineered to have lipase, protease, oxidoreductase and other activities. Thus, one of skill in the art may create an abzyme with the desired characteristics in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed 1/26/10 have been fully considered but they are not persuasive.

Applicant argue that US 4,925,790 teach the use of supercritical fluids for enzymatic reactions and teach the advantages of the use of supercritical fluids over liquid solvents. Applicants argue that trifluoromethane is mentioned as only one of a number of possible fluids to be used in a supercritical state.

While the reference does not exemplify the use of trifluoromethane, it is specifically mentioned as a solvent which is suitable for use in enzymatic reactions. Merely that it is not the preferred solvent, does not eliminate the

teaching of its being a suitable solvent. While it is true that the reference teaches the use of trifluoromethane under supercritical conditions, the claims do not exclude the use of supercritical conditions in the claimed enzymatic process. Please be careful not to include new matter in the response.

Applicant argues that Ferraboschi *et al.* provides no motivation to make use of a hydrofluorocarbon solvent in an enzymatic reaction. Please note, as stated above, the motivation comes from the US 4,925,790 reference where it is stated that any enzyme may be used which include those useful in the production of pharmaceuticals (col. 3, l. 20) particularly with steroids (col. 3, l. 27). Since Ferraboschi *et al.* teach the use of lipase in a resolution of a steroid, this is a clear invitation to substitute the solvent of US '790 in the process of Ferraboschi *et al.*

Careful attention to the construction of the rejection instead of arguing each reference individually might promote prosecution.

One of ordinary skill in the art would have been motivated at the time of invention to make these substitutions in order to obtain the resulting compound as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Evidence of unexpected results with claims commensurate in scope with the showing would be on way to advance prosecution.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is

filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner
Art Unit 1651